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AN EXPERIMENTAL STUDY OF THE ABSORPTION OF STRYCHNINE IN THE DIFFERENT SECTIONS OF THE ALIMENTARY CANAL OF DOGS.*

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The experimental study of the absorption of strychnine from the alimentary canal which I began some years ago on rabbits[1] I have continued on dogs, because it is an indispensable requirement that results which were obtained from experiments upon one class of animals should be tested in experiments on another class of animals before we think of applying such results to the human being, who is the centre of our interest.

Strychnine is available for the study of absorption chiefly on account of its characteristic reaction upon the animal—the appearance of a tetanus is a sure proof of the absorption of a sufficient quantity. The effective doses and the times which elapse between the administration of the poison and the appearance of the tetanus can serve as units for the comparison of the powers of absorption in the different parts of the alimentary canal in the same class of animals.

In such comparisons, of course, the weight of the animal has to be taken into consideration, inasmuch as it might happen that a large dose will not have any effect in a large animal, while a smaller dose may cause a tetanus in a smaller animal. In the experiments which I am now going to present the effective doses of strychnine were reduced to the unit weight of the animal—*i. e.*, in each case the number of milligrammes of strychnine which proved to be effective were divided by the number of kilogrammes of the weight of the animal, thus establishing the number of milligrammes required for each kilogramme of dog to bring out a pronounced tetanus.

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In each experiment the animal was under ether anæsthesia throughout the entire operation.

The sections of the alimentary canal which were thus separately tested for their absorbent power are as follows: Pharynx, œsophagus, stomach, small intestines, large intestine, and rectum.

The report on these separate sections we shall preface, however, with a few experiments in which the strychnine was introduced into the non-isolated stomach of normal animals, where it is, therefore, uncertain in what section of the canal the absorption in these experiments really takes place.

We are now going to let the experiments speak for themselves.

SERIES A.—*Strychnine in the normal stomach.*

EXPERIMENT 1.—A dog, weighing 22 kg., after having fasted for thirty hours, was slightly narcotized, and 22 mg. of strychnine in 50 c.c. of normal salt solution, colored with indigo-carmine, were introduced through a tube into the stomach. The tube was employed, to avoid the contact of strychnine with the mouth, pharynx, etc., and the liquid was stained, in order to recognize its escape. The animal taken from the table had the first tetanic fit just one hour after the administration of the strychnine; a few more fits followed, but the dog survived. In this experiment 1 mg. of strychnine to 1 kg. of dog brought out a tetanus sixty minutes after administration.

EXPERIMENT 2*a*.—A large dog of 35 kg. was given ether; as in the previous experiment, 20 mg. of strychnine were introduced into the stomach. During observation for three hours there was no effect. Here four-sevenths of a milligramme to the kilogramme of dog had no effect.

EXPERIMENT 2*b*.—The same dog, seven days later. I introduced into the stomach, under the same conditions as before, 30 mg. of strychnine. Tetanus appeared after forty minutes, and death occurred forty minutes later. In this case six-sevenths of a milligramme to the kilogramme brought tetanus after forty minutes.

Some more experiments of the same kind were made, but they will not be reported in detail. All these experiments can be reduced to the following average figures: One and one-sixth of a milligramme of strychnine to one kilogramme of dog brings out a tetanus thirty minutes after the introduction of the poison through a tube into the non-isolated stomach of a normal animal. We might remark here that the usual administration of the poison by the mouth is complicated by the fact that it has to come into contact with the mouth, pharynx, etc., where, as it will be shown later, strychnine is absorbed quite readily.

In presenting the experiments on absorption in the separate sections of the alimentary canal we will commence with the small intestines, where, in normal conditions, probably the main absorption takes place. By so doing we shall obtain at the same time a unit by which to measure the absorbent power in the other sections.

As far as I am aware no such experiments were yet made by other investigators to determine the absorption of strychnine from the intestines when introduced into them directly.

SERIES B.—*Strychnine introduced into an isolated loop of the small intestines.*

EXPERIMENT 1.—A dog of 13 kg. was given ether, the intestines exposed and tied at a distance of 12 cm. from the pylorus; an opening was made into the stomach and a tube introduced through the pylorus into the intestine; through this tube 40 mg. of strychnine in 10 c.c. normal salt solution stained with methylene-blue were injected; the tube was then withdrawn and the pylorus rapidly tied. Seven minutes after injection, before the sewing-up of the abdomen could be finished, a tetanus broke out, and the animal died eight minutes later.

In this experiment 3 mg. of strychnine to 1 kg. of dog brought out a tetanus after seven minutes.

EXPERIMENT 2.—A dog of 12½ kg. was given ether, the abdomen opened, a loop of the ileum 12 cm. in length tied at both ends, and 15 mg. of strychnine were injected by a hypodermatic syringe into the empty lumen of the intestinal loop. Tetanus broke out in eleven minutes, and the dog died in twenty-one minutes after the injection. Here 1⅕ mg. of strychnine to 1 kg. of dog brought out a tetanus eleven minutes after the injection.

Here, too, I shall restrict myself to the detailed report of only two illustrative experiments. The average figures are: 1⅖ mg. of strychnine to 1 kg. of dog introduced into a loop of 12 cm. length of the small intestine will bring out a tetanus in ten minutes.

It is probable that in a longer loop the same effect could be obtained by even a smaller dose. I have, however, restricted my experiments invariably to a loop of the same length.

We turn now to that section of the alimentary canal the absorbent power of which has of late often been the subject of investigation—I mean the stomach. We shall restrict the brief historical remarks to the studies made with strychnine. Here we find that Bouley and Colin[2] maintain that it was absorbed quite rapidly in the stomachs of dogs, cats, etc., when the pylorus was tied. Tappeiner[3] finds that in cats the absorbent power of strychnine was retarded in the stomach when the pylorus was tied. In the investigations of these writers the cardia remained open and the animals often vomited. In my experience on rabbits,[4] whose stomachs were ligated at the cardia and the pylorus, no strychnine was ever absorbed from this organ.

In my present experiments on dogs I have studied the absorption from the entire stomach as well as from the fundus alone.

SERIES C.—*Absorption from the isolated stomach.*

EXPERIMENT 1.—A dog weighing 7300 gr. was given ether, the stomach was exposed and the cardia ligated. An opening was made into the duodenum, and through it 20 mg. of strychnine in normal saline solution, colored with methylene-blue, was injected into the stomach by means of a syringe with a long blunt nozzle; the syringe was withdrawn and the pylorus ligated. For two hours and fifteen minutes the dog was observed, but no tetanus appeared, and not even a sign of hyperæsthesia. The dog vomited often, but only white foam without a tinge of blue, a proof that the ligature of the cardia was tight. To prove that the channels of absorption from the stomach were not cut off by the ligatures around the cardia and pylorus, 8 mg. of strychnine in solution tinged with blue were now injected by means of a hypodermatic syringe into the submucous tissue of the anterior wall of the stomach; six minutes later the animal died in a violent tetanic fit while still under ether.

In this experiment 2⅔ mg. of strychnine to 1 kg. of dog had no effect upon the animal.

EXPERIMENT 2.—A dog weighing 10 kg. was etherized; the strychnine was introduced through a tube into a normal stomach. The animal had a tetanus after twenty-five minutes, followed by many other fits, but it survived; 1½ mg. of strychnine to 1 kg. of dog introduced into a normal stomach caused tetanus after twenty-five minutes.

The same dog, five days later, was given ether, the stomach was exposed, the cardia ligated, and we injected through the duodenum into the stomach 30 mg. of strychnine in 50 c.cm. colored saline solution, the pylorus being ligated. It was observed for two hours, but no tetanus, and even no hyperæsthesia appeared. Observation had to be discontinued, and the animal was killed with chloroform.

In this experiment it was conclusively demonstrated that while in the normal stomach of the dog 1½ mg. of strychnine to 1 kg. of dog brought out a tetanus twenty-five minutes after administration of the poison into the stomach, but after ligation of the cardia and pylorus 3 mg. to 1 kg. of dog had no effect whatever. This demonstrates distinctly the pronounced retardation of the absorption in the stomach, comparing it with the absorption in the intestines, where 3 mg. of strychnine to 1 kg. of dog would surely bring out a tetanus in seven or eight minutes.

However, the stomach of the dog differs from that of the rabbit, inasmuch as in the dog large doses of strychnine would bring out a tetanus from the stomach with tied orifices, as can be seen from the following experiments:

EXPERIMENT 3.—Ether was given to a dog weighing 6 kg., the cardia was tied, and I introduced into the stomach through a tube in the pylorus 150 mg. of strychnine in 20 c.c. alcohol (25 per cent.); the pylorus was ligated, the wound sewed up, and the ether discontinued; forty-five minutes later a distinct tetanus broke out, and the animal died after two hours; 25 mg. of strychnine (in alcohol) to 1 kg. of dog brought out a tetanus after forty-five minutes.

I have made a large number of experiments on the absorption from the isolated stomach under varying conditions; either the cardia was first tied and the strychnine was introduced through the pylorus, which was then tied later, or the pylorus was tied first and the strychnine was introduced into the stomach by a tube through the mouth or through an opening in the œsophagus, and then I ligated either the cardia or the œsophagus below the wound. The average figure of all these experiments amount to this: 20 mg. of strychnine to 1 kg. of dog brings out a tetanus forty-two minutes after the introduction of the poison. The smallest dose which was effective in one of these experiments amounted to 9 mg. of strychnine in alcohol to 1 kg. of dog.

The introduction of strychnine into a stomach, the pylorus of which was ligated, but the cardia left open, has not given me clear results, as it was usually complicated by vomiting, which means the bringing of the strychnine into the pharynx, mouth, etc.

I have attempted to study the absorbent power of the fundus of the stomach separately, and the results which I have obtained indicate that the absorptive power is distinctly smaller than that of the entire stomach.

This can be seen from the following experiment:

EXPERIMENT 4.—A dog weighing 5 kg. was etherized, the stomach ligated between the fundus and pyloric portion, cardia ligated, a stomach canula tied tightly in the fundus, and through it 100 mg. of strychnine in an alcohol solution introduced into the fundus. The animal was observed for eighty minutes, but no effect, not even hyperæsthesia, was seen. To prove that the paths of absorption were not cut off by the ligatures, 6 mg. of strychnine were injected into the submucous tissue of the wall of the fundus, and six minutes later a violent tetanus appeared. In this experiment even 20 mg. to 1 kg. of dog could bring out no effect.

We should remark here that the absorption which we have seen readily occurs when the drug is introduced into the non-isolated stomach of normal animals, probably takes place in the intestines; and a part of the interval between the administration of the poison and the appearance of the tetanus seems to be consumed by the time required for the poison to pass in sufficient quantity from the stomach into the intestines.

This accounts for the difference in the length of the intervals of the absorption from the normal stomach and from the intestines.

The opinions which we meet with in the older literature on the absorbent power of the œsophagus are simply guesswork and mostly incorrect. The writer of the chapter on absorption, in the *Classical Handbook of Physiology*, by Hermann,[5] proclaims that "while the food is slowly passing through the œsophagus undoubtedly some of it becomes absorbed there." Berg,[6] who described the well-known case of immense dilatation of the œsophagus observed by Luschka,[7] goes so far as to state that the patient's life was supported by absorption of food from the œsophagus. In the case of chronic cardiospasm, with consecutive dilatation of the œsophagus, which I described some years ago,[8] I demonstrated that atropine or alcohol was never absorbed from the œsophagus. In a similar case recently described by Maybaum,[9] it was established that iodide of potash remained unabsorbed in the œsophagus. In the experiments on rabbits I have shown[10] that the œsophagus of these animals absorbs strychnine very poorly. Similar results were obtained in my present experiments on dogs.

SERIES D.—*Absorption of strychnine from the œsophagus.*

EXPERIMENT 1.—A dog of 7 kg. was etherized, the cardia tied, and I injected into the œsophagus 19 mg. of strychnine. The œsophagus was tied above. After one hundred and forty minutes' observation there was no effect, but the animal was found dead the next morning, aspiration pneumonia being the apparent cause of death; $2\frac{5}{7}$ mg. of strychnine to 1 kg. of dog had no effect.

EXPERIMENT 2.—A dog weighing 4 kg., etherized, was similarly treated. I injected into the œsophagus 20 mg. of strychnine, and tied the œsophagus above. After forty-five minutes a weak tetanus appeared. The dog died after two hours. Here 5 mg. of strychnine to 1 kg. of dog brought out a moderate tetanus after forty-five minutes.

The average figures from all the experiments are: $4\frac{1}{2}$ mg. of strychnine to 1 kg. of dog brought out a tetanus after forty-seven minutes.

We should remember that in these experiments the animal, after awakening from the ether, is swallowing very frequently, and that the peristalsis which follows each deglutition passes under the ligature to the lower parts.[11] The strychnine in the œsophagus is therefore very often subjected to a high pressure, which, of course, facilitates the absorption.

Experiments upon absorption within the pharynx cannot be conducted with desirable precision, since this part cannot be well separated from the mouth, nose, and larynx. The data which were derived from our experiments must indeed be interpreted as an expression of the absorption which takes place in all these parts together, though the bulk of the liquid injected into the pharynx remains there, especially if the animal is kept throughout the experiment on its back, with the head well fixed. Moreover, each experiment was followed up by an autopsy, for the purpose of ascertaining the parts in which the stained solution of strychnine was really located.

SERIES E.—*Strychnine injected into the pharynx.*

EXPERIMENT 1.—A dog weighing 4 kg. was etherized, tracheotomy was performed, and the trachea ligated above; the œsophagus was tied just below the pharynx. I introduced into the pharynx 12 mg. of strychnine in 5 c.c. of a stained solution. Tetanus followed after twenty-five minutes, and death one hour later. Autopsy showed blue saliva mainly in the pharynx, but also in the mouth and in the larynx. In this experiment 3 mg. of strychnine to 1 kg. of dog brought out a tetanus within twenty-five minutes. This can also be taken as an average figure from all the experiments in which tracheotomy was performed. In experiments without tracheotomy the tetanus appeared much earlier after injection and with smaller doses. The autopsies have shown, however, that the blue stain extended deep into the trachea. This observation gave rise to the following experiment:

A dog of 11¼ kg. was etherized, and I injected directly into the trachea 15 mg. of strychnine. Tetanus occurred after six minutes. There were fits, with very short intermissions, until death set in ten minutes later. Here 1⅓ mg. of strychnine to 1 kg. of dog brought out strong tetanic attacks in six minutes.

The absorbent power of the large intestine does not seem to differ materially from that of the small intestines, but the presence of some fecal masses within the colon seems to retard the absorption somewhat, as can be seen in the following experiments:

SERIES F.—*Absorption in the colon.*

EXPERIMENT 1.—To a dog weighing 12½ kg. ether was administered, and the colon, which was not entirely empty, was tied near its junction with the small intestine. An opening was made in the lower part, and 20 mg. of strychnine in a 6 c.c. saline solution injected into the upper part, and the bowel tied immediately. The length of the isolated gut was about 12 cm. The first tetanic fit occurred after twenty-three minutes, the animal dying one hour later. In this experiment 1⅗ mg. of strychnine to 1 kg. of dog produced a tetanus in twenty-three minutes.

EXPERIMENT 2.—A dog of 7½ kg. was given ether and the colon exposed. It was empty. A piece 12 cm. in length was isolated by ligatures, and 10 mg. of strychnine was injected into the lumen of this piece by means of a hypodermatic syringe, and the puncture clamped. The first tetanus appeared nine minutes after the injection, and the animal died after twenty-three minutes. Here $1\frac{1}{8}$ mg. of strychnine to 1 kg. of dog brought out a tetanus after nine minutes.

There have been, however, some variations with regard to doses and time of absorption even in experiments with a perfectly empty colon.

The average figures of these experiments are: $1\frac{4}{5}$ mg. of strychnine to 1 kg. of dog brings out a tetanus in fourteen minutes.

In the experiments upon the rectum we have studied the effect of the injection of strychnine in a non-isolated normal rectum as well as in a rectum which was separated from a colon by means of a ligature. In the first case we are not studying the absorption in the rectum alone, as a part of the injected liquid is surely carried up into the colon or perhaps even into the small intestines.

It deserves to be mentioned especially that in the experiments on the rectum this organ was rarely empty.

On account of the practical importance of these experiments we will describe here in detail a greater number of them.

SERIES G.—*Experiments upon the rectum.*

(*a*) Normal rectum.

EXPERIMENT 1.—Dog of 17 kg.; I injected into the normal rectum 18 mg. of strychnine; after fifteen minutes a tetanic attack broke out; a few more fits followed, but the animal survived. In this experiment $1\frac{1}{17}$ mg. of strychnine to 1 kg. of dog brought out a tetanus after fifteen minutes.

EXPERIMENT 2.—Dog of 22 kg.; I injected 22 mg. of strychnine into the normal rectum. Tetanus occurred after fifteen minutes, and the animal died after an hour. Here again 1 mg. of strychnine to 1 kg. of dog brings out a tetanus after fifteen minutes.

EXPERIMENT 3.—A dog of 23 kg., which received 300 mg. of strychnine in the isolated stomach, was observed for over two hours, but no effect appeared. Now 50 mg. of strychnine was injected through the anus into the rectum; after nine minutes a violent tetanus appeared, and the animal died ten minutes later.

(*b*) Rectum tied about 15 cm. above the anus.

EXPERIMENT 4.—A dog of $11\frac{1}{2}$ kg. was etherized, the rectum tied, and I injected through the anus 20 mg. of strychnine in 6 c.c. of water, colored with methylene-blue; at least one-half of the liquid came out again. Tetanus appeared after fifteen minutes, and death after half an hour. Here about $\frac{4}{5}$ mg. of strychnine to 1 kg. of dog brought a tetanus in fifteen minutes.

EXPERIMENT 5.—Dog of $8\frac{1}{2}$ kg.; after etherization the rectum was tied, and I injected 10 mg. of strychnine into the lumen through the wall of the gut by means of a hypodermatic syringe; the puncture was clamped. After eight minutes a strong tetanus appeared; the animal died after twenty-five minutes. In this experiment 1½ mg. of strychnine brought out a tetanic fit in eight minutes.

EXPERIMENT 6.—A dog of 7 kg. was similarly injected with 20 mg. of strychnine, and the puncture clamped. A violent tetanus broke out after four minutes, and the animal died six minutes later. Here 2⅘ mg. of strychnine brought out a tetanus in four minutes.

EXPERIMENT 7.—A dog of 5700 gr. was etherized, the rectum tied, and I injected through the anus 20 mg. of strychnine in 6 c.c. of colored water; a few drops were expelled. A violent tetanus occurred in two minutes, and death one minute later. In this experiment 3½ mg. of strychnine to 1 kg. of dog gave a tetanus in two minutes.

The average figures from these and other experiments upon the isolated rectum are: 1⅘ mg. of strychnine to 1 kg. of dog brings a tetanus in seven minutes.

In the following three tables a condensed presentation is to be found of the results of the experiments upon the different sections of the alimentary canal. The first table gives that experiment upon each section in which the minimum effectual dose was used. The second table gives the experiment with the shortest interval. The third table gives *average figures* for each series of experiments, which were obtained by the following simple method: The amount in milligrammes of strychnine to the kilogramme of dog, which were employed in every experiment, were added together, and the sum total was divided by the number of experiments made in this series. The same was done with the intervals between the injection and the appearance of the tetanus. All the intervals, in minutes, were added together, and the sum-total was divided by the number of experiments in this series. Both numbers, which were thus composed from all the experiments in each series, were linked together to an average figure which might present at least in an approximate way the absorbent power for strychnine of the corresponding section.

It should be remembered that in starting out to study the absorbent power by means of the characteristic effect of strychnine we had two criteria in mind, by means of which the degree of absorption could be estimated. One of these was the dose which brings out a tetanus, and the other was the time which passes between the administration of the poison and the appearance of the tetanus. Both criteria, the dose and the time, have in common that they are in inverse proportion to the power of absorption—*i. e.*, absorption is increased when they are decreased—in other words, the smaller the dose which can bring on a tetanus, and the shorter the interval between the administration of strychnine and the outbreak of the fit, the greater is the power of absorption of the part in which the strychnine was introduced. But both criteria are in inverse proportion to each other, and cannot be observed during one and the same experiment. The smaller the dose which can effect a tetanus the longer is the interval between the appearance of the tetanus and the administration of strychnine, and, on the other hand, in order to obtain a shorter interval a larger dose has to be employed. However, by compounding average figures from the entire series of experiments with the minimum dose, as well as those with the shorter intervals, we obtain a measure for the absorbent power in which both criteria are equally represented. We can now state that the first table presents the power of absorption as adjudged by the criterion of the dose, the second table that judged by the criterion of the interval, and the third table shows the absorbent power as compounded from both criteria together.

TABLE I.—SHOWS THE EXPERIMENTS WITH THE EFFECTIVE MINIMUM DOSES OF STRYCHNINE IN MILLIGRAMMES REDUCED TO 1 KILO OF DOG.

Section of alimentary canal.	*Strychnine.*	*Interval between injection and tetanus.*
Normal stomach	$\frac{6}{7}$ mgr.	40 minutes.
Small intestines	1 “	13 “
Isolated stomach	9 “	20 “
Œsophagus	4 “	50 “
Pharynx	$1\frac{2}{3}$ “	20 “
Colon	$1\frac{1}{3}$ “	9 “
Rectum	$\frac{4}{5}$ “	15 “

TABLE II.—SHOWS THE EXPERIMENTS WITH SHORTEST INTERVAL BETWEEN INJECTIONS AND APPEARANCE OF TETANUS.

Section of alimentary canal.	*Strychnine.*	*Interval between injection and tetanus.*
Normal stomach	$1\frac{1}{2}$ mgr.	25 minutes.
Small intestines	$2\frac{1}{2}$ “	8 “
Isolated stomach	23 “	15 “
Œsophagus	5 “	45 “
Pharynx	$1\frac{2}{3}$ “	20 “
Colon	$1\frac{3}{4}$ “	8 “
Rectum	$3\frac{1}{2}$ “	2 “

TABLE III.—AVERAGE FIGURES.

Section of alimentary canal.	*Strychnine.*	*Interval between injection and tetanus.*
Normal stomach	$1\frac{1}{6}$ mgr.	31 minutes.
Small intestines	$1\frac{2}{5}$ “	10 “
Isolated stomach	20 “	42 “
Œsophagus	$4\frac{1}{2}$ “	47 “
Pharynx	3 “	25 “
Colon	$1\frac{4}{5}$ “	14 “
Rectum	$1\frac{4}{5}$ “	7 “

I believe that the experiments embodied in this paper have established the following points:

The absorption of strychnine in the stomach is incomparably lower than in any other section of the alimentary canal, and, furthermore, the absorbent power of the fundus seems to be even lower than that of the entire stomach.

The power of absorption in the œsophagus is somewhat better than in the stomach, but is still considerably inferior to the absorption within the other parts of the alimentary canal.

The power of absorption in the other three parts of the canal—*i. e.*, the small intestines, colon, and rectum—seems to be equal. The differences which were observed are too small and the method not exact enough to justify the assumption of an actual difference in the absorbing power of these parts. However, these experiments brought out the following remarkable facts: that the isolated rectum absorbs at least as well as the small intestines; that in some experiments the effects appeared earlier when the rectum was isolated than when it had free connection with the balance of the gut; that from no part of the canal were such short intervals between the injection of the strychnine and the appearance of the tetanus observed as were frequently seen when it was injected into the rectum—in the latter case the interval was sometimes only two or three minutes; finally, impaction of the rectum proved to be no hinderance to the prompt absorption of the poison therefrom.

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A CRITICAL SUMMARY OF THE LITERATURE

ON

SPLENIC PSEUDOLEUKÆMIA (ANÆMIA SPLENICA; SPLENOMEGALIE PRIMITIVE).[1]

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HISTORY OF THE DISEASE. The history of splenic pseudoleukæmia is inseparably connected with that of the diseases to which it is closely allied—namely, leukæmia and the other forms of pseudoleukæmia. Its study, therefore, may well trace the development of our knowledge of those diseases as a class. The attention of the medical profession was early directed to a complexus of symptoms characterized by enlargement of the spleen, pallor, hemorrhages, œdema, and grave cachexia. Hippocrates wrote on the association of splenic tumor with dysentery, hemorrhage, scorbutus, and miasmatic diseases. Galen described hypertrophy of the spleen in protracted autumnal fever and other cachectic states. Malpighi, Morgagni and others observed splenic and lymphatic enlargement associated with pallor, hemorrhage, and emaciation, which progressed to a fatal termination. Nivet[1] mentions scorbutus, rhachitis, and scrofula among the many causes of splenic enlargement. In some of the cases of splenic hypertrophy reported by him under the heading of rhachitis and scrofula, extensive glandular enlargement and grave cachexia developed during the course of the disorders. There is much in the literature of the older writers to indicate that they were quite familiar with hypertrophy of the spleen in miasmatic disease, and that they also had noted the condition in various other affections, such as scrofula, continued fevers, syphilis, and liver disease. Now and then one also finds record of cases in which, without apparent cause, the spleen enlarged, hemorrhages and cachexia supervened, and death followed. No particular types of disease of this nature were well recognized, however, until, in 1832, Hodgkin wrote his now well-known article on "Some Morbid Appearances of the Absorbent Glands and Spleen."[2] He reported a number of cases which showed an increase in the size of the lymph-glands and spleen, followed by emaciation, ascites, pallor, œdema, and death. The blood was not examined in any of the cases, and the report in many instances is meagre. One is able to discern, however, that undoubtedly the author's cases included carcinoma, tuberculosis, sepsis, and probably other morbid conditions. Nevertheless, it was the first worthy attempt to group this class of affections. In October, 1845, Bennet published the report of a case of hypertrophy of the spleen in which the blood of the patient contained a great number of white corpuscles resembling pus-cells. In November of the same year Virchow reported a similar case, and correctly attributed the large increase in the white cells to an augmentation of the white blood-corpuscles. He believed that the great increase in the leucocytes was due to the hypertrophy of the spleen. Subsequently, he evolved the doctrine of the disease, leukæmia, which he described as an affection characterized by cachexia, enlargement of the spleen and lymph-glands, and an augmentation in the number of white blood-corpuscles. Other histological changes of the disease described by him were cellular hyperplasia of the lymph-glands and spleen and infiltration of lymph-cells

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[1] For the author's report of a case, see THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, October, 1899, vol. cxviii., No. 330, p. 428.

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[1] Archives Generales de Medicine, 1838.

[2] Medico-Chirurgical Transactions.